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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/519,174

09/01/2005

Ralf Herwig

13027.60USWO

5243

23552 7590 05/11/2010

MERCHANT & GOULD PC

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MINNEAPOLIS, MN 55402-0903

EXAMINER

NATARAJAN, MEERA

ART UNIT

PAPER NUMBER

1643

MAIL DATE

DELIVERY MODE

05/11/2010

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/519,174	HERWIG, RALF	
	Examiner	Art Unit	
	MEERA NATARAJAN	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 17 September 2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-6 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-6 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>10/16/2008</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 09/17/2009 has been entered.
2. Accordingly, Claims 1-6 are pending and will be examined on the merits.

Claim Rejections Maintained - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. The rejection of Claims 1-6 under 35 U.S.C. 102(b) as being anticipated by Brandt et al. (Cancer Research, Vol. 56, pp.4556-4561, 1996) is maintained.
5. The claims are drawn to a method and a kit for determination of characteristics and/or classification of circulating macrophages comprising the steps of taking a whole blood sample subjecting it to gradient centrifugation for isolating macrophages and/or peripheral mononuclear blood cells, perforating said cells and staining with a PSA

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antibody, followed by flow cytometric analysis for statistical evaluation of the cell contents.

6. Brandt et al. teach isolation of prostate-derived single cells and cell clusters from human peripheral blood. Brandt et al. teach a cytokeratin immunomagnetic method of isolating PSA-positive epithelial cells from the circulating blood of prostate cancer patients as a means to analyze genetic and biochemical characteristics of such cells for clinical relevance of prostate cancer cell identity and risk of metastasis (see p.4558 last paragraph and p.4561 last paragraph). Peripheral blood samples from patients were gradient centrifuged (see materials and method p.4556, right column, lines 30-31) and permeabilized using saponin (see materials and method p.4556 line 49) after which they were stained with antibodies directed to PSA, CD45, or CD14 (see p.4557 right column, lines 9-13). Flow cytometric analysis was then performed to sort the cells (see Fig. 1, p. 4558). The reported isolation method yielded prostate-derived cells or clusters of them from prostate cancer diagnosed patients (see Abstract). Specifically flow cytometric analysis revealed mononucleated cells, granulocytes, lymphocytes and monocytes in the peripheral blood of patients (see p.4558, Fig. 1a). The reference teaches each and every limitation of the claims.

Response to Arguments

7. Applicants argue the methods of Brandt et al. do not isolate macrophages either through density gradient centrifugation or immunomagnetical separation. Applicants argue the method of Brandt et al. utilizing density gradient centrifugation actually excludes macrophages from the isolation procedure by eliminating the single band of

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cells between the interface of the plasma. In addition, Applicant's point out an "analysis of macrophages is not performed in Brandt et al., and can be seen that on the Figures on page 4558, areas R1-R4 do not show macrophages, but only mononucleated cells, granulocytes, lymphocytes and monocytes". These arguments have been carefully considered but not found persuasive.

8. Brandt et al. describe the method of gradient centrifugation as the following: "A column of 5 ml of EDTA-treated blood drawn from patients was laid on top of the gradient. The tube was centrifuged at 450 X g in a bench centrifuge for 20 min at room temperature. The single band of cells between the interface of the platelet-enriched plasma and density of 1.068 g/ml was removed. The removed cells were pelleted by centrifugation at 200 X g. The harvested cells from the single band at the interface of the platelet-enriched plasma and the 1.068 NycoPrep density medium were fixed in 1 ml of a paraformaldehyde/PBS fixative for at least 2 h at room temperature...". The method goes on to recite the harvested cell suspension was incubated with a medium containing saponin (to perforate the cells). The Applicant's argument is incorrect, the cells "removed" are actually the cells that are used for the staining. They are not discarded. Applicants additional argue that Brandt et al. do not show analysis of macrophages, but only show mononucleated cells, granulocytes, lymphocytes and monocytes. It is well known in the art that monocytes represent the circulating macrophage population and should be considered fully functional for their location. Monocytes are essentially circulating macrophages in the blood and since the claim is directed towards a method of isolating "macrophages" from the blood (and not tissue)

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one of ordinary skill in the art would consider isolating monocytes (shown in R4 of Fig. 1a) to read on the claim. Therefore, the rejection of record is maintained.

All previous rejections are withdrawn in view of Applicant's amendments in the reply filed on 09/17/2009.

Conclusion

9. Claims 1-6 are rejected.

10. No Claim is allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to MEERA NATARAJAN whose telephone number is (571)270-3058. The examiner can normally be reached on Monday-Thursday, 9:30AM-7:00PM, ALT. Friday. EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic

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Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

MN

/Larry R. Helms/
Supervisory Patent Examiner, Art Unit 1643